

DESIGN AND DEVELOPMENT OF AN AUTOMATED METERED DOSE
INHALER (MDI) FOR ASTHMATIC PATIENT

TSEN VUI HIN

A thesis submitted in
fulfillment of the requirement for the award of the
Degree of Master of Electrical Engineering

Faculty of Electrical and Electronic Engineering
Universiti Tun Hussein Onn Malaysia

JULY 2018

For my beloved parent and family, friends, supervisor and co-supervisor, thank you.



ACKNOWLEDGEMENT

Firstly, I would like to express my sincerely heart gratitude to the Almighty God for the wisdom, knowledge and perseverance that God has bestowed me during this research and even though in my life.

Foremost, I would like to thank Universiti Tun Hussein Onn Malaysia for funding this project under UTHM short term grant (STG) Vot. U350 and *Geran Penyelidikan Pascasiswazah* (GPPS) grant Vot. U587.

I would like to express my deepest gratitude to my supervisor and my co-supervisor, Dr. Nur Ilyani Binti Ramli and Dr. Farhanahani Binti Mahmud, for their excellent guidance, caring, patience, motivation, and immense knowledge to help me in all the time of research and writing of this thesis. Without them, the completion of this thesis and this research are unlikely possible.

Besides my supervisor and co-supervisor, I also would like to thank all the department faculty members for their help and other lecturers throughout this research. Furthermore, I also would like to thanks Mybotic for always help me to order electronic components and support while I'm trouble in programming. I acknowledge, with appreciation, Dr. Nur Iyani Ramli and Dr. Audrey Huong for offering me the convenience facility such as furniture in this research.

Not to be forgotten, I would like to thankful to Pia Chia Pei Qin for always support me in physically and spiritually for this thesis writing. Therefore, thousand thanks to and appreciations to my friends who are, Kang Huai, Ong, Syukri, Afif, Sheena, and everyone who involved help me directly and indirectly in this research.

Finally, I would like to express the deepest appreciation to my beloved parents and family whose have greatly tolerant, supportive and precious love throughout the completion of this research and thesis.

ABSTRACT

To date, infant with illness associated with the pulmonary airway is treated by a doctor using a spacer device with metered dose inhaler (MDI) to allow the infant to breathe in the medication known as salbutamol. Current asthma spacer does not provide systematic way of monitoring and displaying the percentage value of the propellant. Furthermore, user non-compliance is found to contribute towards longer recovery rate. Therefore, this product is designed and developed capable of detecting the propellant level inhaled by the infant by using a MQ-6 gas sensor and monitoring its percentage value. The display of available puffs of MDI canister and the battery indicator for the system are also included in the device. The automated actuation MDI was required a push button to press the MDI canister where this project utilised Arduino Nano as the microcontroller to control the system operation and all the reading values will be displayed on the OLED. RGB LED is also used to visualise the propellant level. The obtained results of the detection of propellant in voltage from the MQ-6 gas sensors were analysed in MATLAB to make comparison through the obtained results. Without propellant, voltage recorded is $0.640 \pm 0.024V$ whereas high concentration of propellant displayed voltage of $1.126 \pm 0.020V$. The mean standard error rate of propellant detection is 5.584%. The first design of the actuation device and interface monitoring display of automated MDI were recorded the highest percentage which is 75% and 80%. The concentration of propellant depends on the ambient temperature due to the MQ-6 gas sensor required minimum working temperature between $20^{\circ}C$ to $22^{\circ}C$. The mean weight of the MDI canister for each puff is 6.257mg and the standard deviation is 3.629mg. Due to experiment conducted, the speed and pressure of pressing MDI canister causes variability in the released of salbutamol and propellant. Observation proved that ambient temperature and propellant released amount also influenced the final reading from the automated actuation MDI.

ABSTRAK

Sehingga kini, bayi yang menghadapi penyakit yang berkaitan dengan paru-paru akan dirawat menggunakan *spacer device* dengan *metered dose inhaler* (MDI) oleh doktor untuk membolehkan bayi bernafas dalam ubat yang dikenali sebagai salbutamol. *Asthma spacer* semasa tidak menyediakan cara pemantauan yang sistematik dan memaparkan nilai peratusan propelan dalam masa sebenar. Selain itu, ketidakpatuhan pengguna didapati menyumbang kepada kadar pemulihan yang lebih lama. Oleh itu, produk ini direka dan dibangunkan yang mampu mengesan tahap propelan yang disedutkan oleh bayi dengan menggunakan pengesan gas MQ-6 dan memantau nilai peratusannya secara dalam masa sebenar. Paparan *available puffs MDI canister* dan penunjuk bateri untuk sistem juga dimasukkan di dalam peranti ini. *Automated actuation MDI* memerlukan butang tekan untuk menekan *MDI canister* di mana projek ini menggunakan Arduino Nano sebagai pengawal mikro untuk mengawal operasi sistem dan semua nilai bacaan akan dipaparkan pada OLED. RGB LED juga digunakan untuk menggambarkan tahap propelan. Keputusan yang diperolehi dari pengesan gas MQ-6 dalam voltan dianalisis di MATLAB untuk membuat perbandingan melalui keputusan yang diperolehi. Tanpa propelan, voltan yang direkodkan adalah di antara $0.640 \pm 0.024V$ manakala kepekatan tinggi propelan menunjukkan voltan $1.126 \pm 0.020V$. Kadar piawai kesilapan min pengesanan propelan ialah 5.584%. Rekabentuk pertama peranti penggerak dan pemantauan paparan telah mencatat peratusan tertinggi iaitu 75% dan 80%. Kepekatan propelan bergantung kepada suhu ambien kerana pengesan gas MQ-6 memerlukan suhu kerja minimum di antara 20°C hingga 22°C. Purata berat *MDI canister* untuk setiap sedutan adalah 6.257mg dan sisihan piawai adalah 3.629mg. Bergantung eksperimen yang telah dijalankan, kelajuan dan tekanan menekan *MDI canister* akan menyebabkan kebolehubahan dalam pelepasan salbutamol dan propelan. Pemerhatian membuktikan bahawa suhu ambien dan jumlah propelan juga mempengaruhi pembacaan akhir dari *automated actuation MDI*.

CONTENTS

TITLE	i
DECLARATION	ii
DEDICATION	iii
ACKNOWLEDGEMENT	iv
ABSTRACT	v
ABSTRAK	vi
CONTENTS	vii
LIST OF TABLES	xii
LIST OF FIGURES	xiii
LIST OF SYMBOLS AND ABBREVIATIONS	xvii
LIST OF APPENDICES	xxi
 CHAPTER 1 INTRODUCTION	 1
1.1 Background of study	1
1.2 Problem statement	2
1.3 Aim	4
1.4 Objectives	4
1.5 Scopes of research	5
1.6 Contributions of the research	6
1.7 Thesis organisation	7

CHAPTER 2 LITERATURE REVIEW 8

2.1	Statistics of asthma in Malaysia	10
2.2	Respiratory airways	11
2.2.1	Trachea	12
2.2.2	Bronchial “tree”	13
2.2.3	Respiratory airways pressure	14
2.3	Normal lungs function in infant	15
2.4	Lung condition when under asthma attack	16
2.4.1	Asthma in infant	16
2.5	Current treatment asthma at home	17
2.5.1	Metered dose inhaler (MDI)	18
2.5.2	Nebulizer	22
2.5.3	Comparison of MDI and nebulizer	23
2.6	MDI products for asthmatic patients	24
2.6.1	MDI with counter available in market	24
2.6.2	Actuation device in MDI	28
2.7	Previous works for usage of gas sensor	33
2.8	Gas sensing methods and material	34
2.8.1	Gas sensing method based on electrical properties	34
2.8.1.1	Metal oxide semiconductor	35
2.8.1.2	Polymer	36
2.8.1.3	Carbon nanotubes	37
2.8.1.4	Moisture absorbing material	37
2.8.2	Gas sensing method based on other properties	38
2.8.2.1	Optic methods	38
2.8.2.2	Acoustic methods	39

2.8.2.3	Gas chromatograph	39
2.8.2.4	Calorimetric methods	40
2.8.3	Summary of different gas sensing methods	42
2.9	Hardware apparatus	43
2.9.1	Arduino Nano	43
2.9.2	Gas sensor (MQ-6)	44
2.9.3	DC micro metal gear motor	47
2.9.4	Organic light-emitting diode (OLED)	48
2.10	Summary	49
CHAPTER 3	RESEARCH METHODOLOGY	50
3.1	Development of electronic segment	53
3.1.1	Block diagram of proposed device	53
3.1.2	Block diagram of automated actuation device	55
3.1.3	Operation system of proposed device	55
3.1.4	Connection of schematic diagram for proposed device	59
3.1.5	Printed circuit board (PCB) for the proposed device	61
3.2	Development of mechanical segment	65
3.2.1	Actuation device utilise gear method	65
3.2.2	Actuation device utilise counterweight method	67
3.2.3	Development of housing for circuit	69
3.2.4	The proposed design of automated MDI	71
3.2.4.1	Mechanical design of automated MDI actuation device	71
3.2.4.2	Monitoring display of automated MDI	74
3.3	Experimental setup	76

3.3.1	Experimental setup for MQ-6 gas sensor	76
3.3.2	Experiment setup of counter of available puffs	79
3.4	Summary	81
CHAPTER 4	RESULTS AND DISCUSSION	82
4.1	Results of electronic segment	83
4.2	Results of mechanical segment	89
4.2.1	Results of proposed design of automated MDI	92
4.3	Prototype of automated actuation device	96
4.4	Result of experimental setup	97
4.4.1	Detection of propellant	97
4.4.2	The counter for salbutamol	100
4.5	Discussion	102
4.5.1	Detection of propellant	102
4.5.2	The counter for salbutamol	104
4.5.3	Percentage of battery	105
4.5.4	Mechanical segment	105
4.6	Summary	107
CHAPTER 5	CONCLUSION AND RECOMMENDATION	108
5.1	Conclusion	108
5.2	Recommendation	110

REFERENCES	111
APPENDIX	121
VITA	158



LIST OF TABLES

2.1	Summary of maximum inspiratory and expiratory pressures	14
2.2	Device and formulation variables that influence drug delivery from MDI [51]	19
2.3	Summary differences between MDI and nebulizer	23
2.4	Summary the products of MDI available in market	27
2.5	Summary of the previous works of using gas sensor	33
2.6	Summary of gas sensing method with different materials	42
2.7	Properties of Arduino UNO	44
2.8	Standard work condition for MQ-6 gas sensor [87]	45
2.9	Sensitivity characteristics for MQ-6 gas sensor [87]	45
2.10	Technical specifications for DC micro metal gear motor	47
4.1	Minimum and maximum output voltage of MQ-6 gas sensor without and concentrated with propellant	97
4.2	A comparison of detection of propellant between the initial, peak and ending voltage	98
4.3	Mean and standard deviation of initial, peak and ending voltage of propellant detection	99
4.4	Summary of mean, standard deviation and error of detection of propellant	99
4.5	The value of available puffs and weight of MDI canister	101
4.6	Observation of experiment for MQ5 and MQ-6 gas sensor	103

LIST OF FIGURES

1.1	Flow-Vu® Inspiratory Flow Indicator (IFI) [18]	3
2.1	Overall of related literature review	9
2.2	The diagram of respiratory airways (major airways) [22]	11
2.3	The diagram of (a) trachea [24] (b) cross section of trachea [25]	12
2.4	The diagram of bronchioles "tree" with alveoli [28]	13
2.5	The diagram of lungs [34, 35]	16
2.6	Pathology of asthma in infant [43]	17
2.7	(a) MDI (Asthalin) (b) Asthma spacer (Aero Chamber)	18
2.8	The internal structure of metered dose inhaler [52]	19
2.9	A unit of MDI canister contains 200 puffs of salbutamol	21
2.10	An example uses of asthma spacer to take inhalation of salbutamol	21
2.11	Diagram of nebulizer	22
2.12	The diagram of low-cost smart inhaler counter with inhaler APP [63]	24
2.13	PuffMinder Doser [64]	25
2.14	SmartTouch Ventolin monitor [65]	26
2.15	MDI mechanical dose indicator [68]	27
2.16	(a) Top-down view of the recording rig showing FSR on canister (b) Side view of recording rig showing microphone placement [70]	28
2.17	Side view of the first design of actuator device [71]	29
2.18	Side view of the second design of actuator device [71]	30
2.19	Side view of the third design of actuator device [71]	31
2.20	Crank shaft of a vehicle	32

2.21	Classification of gas sensing methods [79]	34
2.22	Schematic diagram of catalyst sensor and configuration of ceramic bead	40
2.23	Labelled Arduino Nano board	43
2.24	Module of MQ-6 gas sensor	44
2.25	Basic circuit of MQ-6 gas sensor [87]	46
2.26	DC micro metal gear motor	47
2.27	Organic light-emitting diode (OLED) 0.96-inch	48
3.1	Overall flow of project methodology	52
3.2	Block diagram of proposed device	53
3.3	Block diagram of automated actuation device	55
3.4	Flow chart of system operation for battery indicator, reset counter value, sub process for	57
3.5	Flow chart of system operation for counter available puff	58
3.6	Full schematic diagram of proposed device	59
3.7	(a) Top view of first board of PCB, (b) rear view of first board of PCB	62
3.8	(a) Top view of third board of PCB, (b) rear view of third board of PCB	63
3.9	Internal of MDI housing utilised gear method	65
3.10	Labelled rotation of gear in MDI housing	66
3.11	Internal of MDI housing	67
3.12	Labelled of rotation of counterweight	68
3.13	Overall housing circuit	69
3.14	(a) Rear view of circuit housing, (b) bottom view of circuit housing	69
3.15	First design of automated MDI actuation device (Graphical)	72
3.16	Second design of automated MDI actuation device (Graphical)	72
3.17	Third design of automated MDI actuation device (Graphical)	73
3.18	First design of monitoring display of automated MDI	74
3.19	Second design of monitoring display of automated MDI	75

3.20	Third design of monitoring display of automated MDI	75
3.21	Block diagram of analytical method	77
3.22	Add-ons package for Arduino	78
3.23	Experiment setup of analogue signal acquisition	79
3.24	Precision Weighing Balances (A&D Weighing GR-200 lab balance)	80
4.1	Electronic components segment	83
4.2	The circuit of the automated actuation device	84
4.3	Three boards of PCBs circuit of the automated actuation device	85
4.4	Pictures are showing (a) initial state of gas sensor (No propellant) (b) gas sensor had detected 100% of propellant (c) 50% of propellant have been inhaled (d) 100% of propellant have been inhaled	86
4.5	High level of available puff in MDI canister	87
4.6	Moderate level of available puff in MDI canister	87
4.7	Low level of available puff in MDI canister	88
4.8	(a) Empty canister of MDI, (b) indicator of percentage of battery	88
4.9	Internal view of actuation device	89
4.10	(a) The counterweight pressed the MDI canister (b) the counterweight is depressed the MDI canister	90
4.11	Prototype of overall housing circuit	91
4.12	Bottom view of prototype of overall housing circuit	91
4.13	Statistics of experiences of asthma	92
4.14	Statistics of handedness for daily activities	93
4.15	Statistics of actuation device	93
4.16	Statistics of interface of monitoring display of actuation device	94
4.17	The reason of the arrangement interface monitoring display	95
4.18	Prototype of automated actuation device	96
4.19	Summary of detection of propellant	98
4.20	Mean and standard deviation of detection of propellant	99

4.21	The level of propellant versus available puff in the MDI canister	100
4.22	The relationship between the available puffs and the weight of MDI canister	101
4.23	Mean and standard deviation of the weight of the MDI canister	102
4.24	The size of the teeth of the gear	106



LIST OF SYMBOLS AND ABBREVIATIONS

A	–	Ampere
AC	–	Alternating Current
ADC	–	Analogue to digital conversion
AED	–	Atomic emission detection
APP	–	Application
CFC	–	Chlorofluorocarbons
CH ₄	–	Methane
cm	–	centimetre
cmH ₂ O	–	centimetre of water
CNT	–	Carbon nanotube
CO	–	Carbon monoxide
CO ₂	–	Carbon dioxide
COPD	–	Chronic Obstructive Pulmonary Disease
CPAP	–	Continuous positive airway pressure
DC	–	Direct Current
DOAS	–	Differential optical absorption spectroscopy
EEPROM	–	Electrically Erasable Programmable Read-Only Memory
EN	–	Enable
GSM	–	Global System for mobile communications
H ₂ O	–	Hydrogen oxide
HFA	–	Hydrofluoroalkane
I/O	–	Input/Output
I ² C	–	inter-integrated circuit
IC	–	Integrated circuit
IDE	–	Integrated Development Environment

IFI	–	<i>Flow-Vu®</i> Inspiratory Flow Indicator
IR	–	Infrared
KB	–	Kilo Byte
Kg	–	Kilogram
K Ω	–	Kilo ohm
LCD	–	Liquid crystal display
LED	–	Light Emitting Diode
LIBS	–	Laser-induced breakdown spectroscopy
LIDAL	–	Raman light detection and ranging
LPG	–	Liquefied Petroleum Gas
LPN	–	Liquefied Natural Gas
mA	–	Milliampere
mbar	–	Millibar
MDI	–	Metered Dosed Inhaler
MHz	–	Mega hertz
mW	–	Milliwatt
MWCNTs	–	Multiwall carbon nanotubes
NH ₃	–	Ammonia
NO _x	–	Nitrogen oxide
OLED	–	Organic light emitted diode
PAni	–	Polyaniline
PCB	–	Printed Circuit Board
PD	–	Partial discharge
PFPD	–	Pulse flame photometric detection
P _H	–	Heating consumption
PLA	–	Polylactic Acid
pMDI	–	Pressurized metered dose inhaler
Ppth	–	Parts-per-thousand
PPy	–	Polypyrrole
PTh	–	Polythiophene
PWM	–	Pulse Width Modulation

RFID	–	Radio-frequency identification
RGB	–	Red, Green. Blue
R_H	–	Heater resistance
R_L	–	Load resistance
RPM	–	Resolutions per minute
SCD	–	Sulphur chemiluminescence detection
SCL	–	Clock line
SDA	–	Data line
SF_6	–	Hexafluoride gas
SIL	–	Single in line
SMT	–	Surface mounted technology
SnO_2	–	Tin oxide
SPI	–	Serial Peripheral Interface
SRAM	–	Static random-access memory
SWCNTs	–	Single-walled carbon nanotubes
TC	–	Thermal conductivity
TDLAS	–	Tunable diode laser absorption spectroscopy
TNB	–	<i>Tenaga Naional Berhad</i>
USB	–	Universal serial bus
V	–	Voltage
val	–	Digital signal from MQ-6 gas sensor
V_C	–	Circuit voltage
V_H	–	Heating voltage
V_{in}	–	Input voltage
VOCs	–	Volatile organic compounds
WSNs	–	Wireless Sensor Network
x	–	Minimum value of digital signal from MQ-6 gas sensor
y	–	Different value of digital signal from MQ-6 gas sensor
β_2	–	Beta 2
%	–	Percent
μF	–	Micro Farad

3D	–	Three dimensional
°C	–	Degree Celsius



LIST OF APPENDICES

APPENDIX	TITLE	PAGE
A	2D drawing of actuation device	121
B	2D drawing of overall design circuit housing	131
C	Graphical detection of propellant	140
D	Different view of PCB boards	145
E	Different view of prototype	149
F	Questionnaire	152
G	Inform consent form	155
H	List of associated publications	156



PTTA UTHM
PERPUSTAKAAN TUNKU TUNJUKAN AMINAH

CHAPTER 1

INTRODUCTION

This chapter is structured as the follow: background of study for asthma in section 1.1 and section 1.2 presented the problem statement. The aim and objectives of this research are presented in section 1.3 and 1.5. The scopes of this work present in section 1.5. Lastly, the contribution of the research and thesis organisation are mentioned in section 1.6 and 1.7.

1.1 Background of study

To date, the common problem in healthcare industry is the diagnosis of disease precisely at inexpensive price [1]. According to the Global Asthma Report 2014, around 334 million of people in the global suffering from asthma [2, 3]. In Malaysia scenario shows that five percent of adults have asthma, while children recorded 10 percent but the numbers are growing over the years [4]. Asthma is the leading chronic childhood disease with albatross on affected children and their families [5, 6]. It occurs when the pulmonary airway is blocked or the airways become narrowed. This may affect the person and result in difficult breathing and shortness of breath [7]. Pulmonary airway is the channel that oxygen and carbon dioxide passes through before or after entering the lungs [8]. The diameter of the channel or the size of the channel for the gasses to pass through it is known as pulmonary airway calibre. If asthma attack is severe the person need to take an emergency treatment to restore the normal breathing.

A study shows that asthma disease is the most frequently occurs in town or city than rural community [5, 9, 10]. Asthma more occurs in urban areas due to often there are haze and air pollution such as fumes from vehicles, factories and so on. Asthma can categorized into two categories which are allergic asthma and non-allergic asthma. In Malaysia, around 80 percent to 90 percent people suffers allergic asthma where it mostly occurs in infant, children and young adults [11, 12]. In Malaysia context analysis shows that the response of the allergic asthma is caused by house-dust, cockroach, cat dander or dog epithelium and cow milk, soya bean, egg, peanut, fish, shrimp, crab, banana and wheat [12].

The effective of air flow in human body depends on the pulmonary airway calibre. Abnormal changes in the size of pulmonary airway calibre will cause Chronic Obstructive Pulmonary Disease (COPD) and asthma. Adult patients normally use metered dose inhaler (MDI) to take inhalation of salbutamol through the mouth to recover from the asthma attack due to the MDI only require to shake for 10 seconds before use it [13]. For infant of the age one to twelve months who are unable to speak, when experiencing the asthma attack they also require dosage of salbutamol to recover from asthma attack. However, infants are unable to use the inhaler to take salbutamol directly because they are unable to inhale. In this case, normally doctor or medical staff will use asthma spacer (aero chamber) together with the salbutamol to recover from asthma attack [14].

1.2 Problem statement

The COPD and asthma are the health condition as a result in lack of oxygen entering the lungs. This will cause shortness in breath and if left untreated it can lead to death. For infant with illness associated with the pulmonary airway, doctor will use an asthma spacer device with MDI to allow the infant to breathe in the medication known as salbutamol [14]. It is a short-acting β_2 -adrenergic receptor against use for the relief of bronchospasm which helps to relax the smooth muscles in the air passages in the lungs, opening the airways to assist breathing. When using the asthma spacer to inhale the salbutamol, some infant is frightened by the mask and fight the treatment [15]. The use of this device is

inconvenient among parents when giving treatment due to the application of the corresponding device which is bound to cause discomfort in infants.

Research has shown that drug delivery is highly dependent on the patient's inhaler technique and ability of inhalation of propellant [16]. Therefore, it is difficult for the infant since they have not developed the technique and ability to properly inhale the salbutamol. In addition, it is also difficult to coordinate actuation within the inhalation when using MDI and asthma spacer. All the problems stated may result in insufficient amount of salbutamol inhaled by the infant and low lungs deposition of the medication [16].

Furthermore, current asthma spacer only indicates manually the inhalation of salbutamol by using *Flow-Vu*® Inspiratory Flow Indicator (IFI) as shown in Figure 1.1. After the MDI canister is pressed, parent required manually to count the number of *Flow-Vu* indicator reaches to 5 flips to 6 flips [17] where maintain seal 5 breaths to 6 breaths. The *Flow-Vu* indicator is moving forward and reverse during the inhalation of salbutamol. Hence, this problem was very cumbersome where the parent required manually to count the number of flipped by the *Flow-Vu* indicator. Therefore, there is no systematic method of monitoring the level of propellant in the asthma spacer after the MDI canister is pressed. Hence, a systematic device to monitor the level of propellant in the asthma spacer will be develop to overcome the problems as been listed.

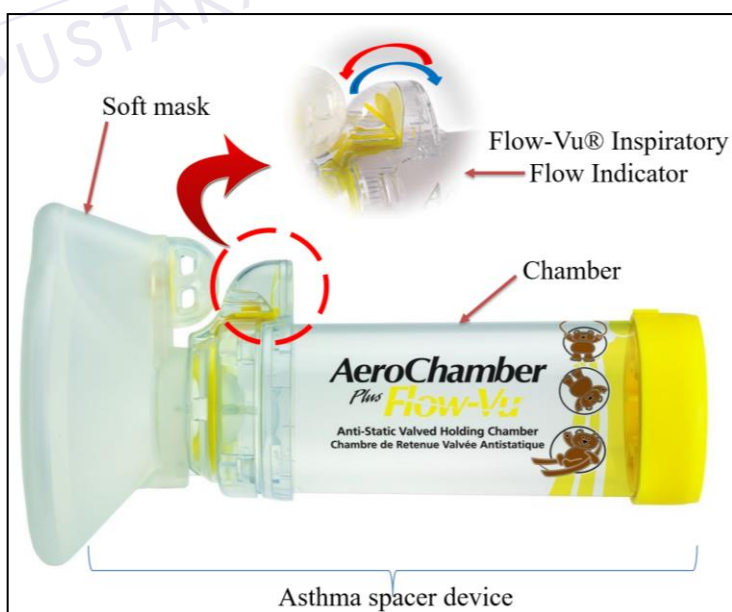


Figure 1.1: Flow-Vu® Inspiratory Flow Indicator (IFI) [18]

1.3 Aim

The aim of this research is to design and develop of an automated actuation device for MDI capable of monitoring the level of propellant in asthma spacer inhaled by infant and to count the available puffs in the MDI canister.

1.4 Objectives

The objectives of this research are as follows:

- a) To design operation system which capable of monitoring the level of propellant inhaled by infant, a counter to represent the number of puffs available in MDI canister and RGB LED as visualisation to indicate the level of salbutamol in MDI canister.
- b) To develop a prototype for asthma spacer with a automated actuation device for metered dose inhaler (MDI).
- c) To analyse the obtained results from gas sensor and counter for available puffs.

REFERENCES

- [1] S. Aneja and S. Lal, "Effective asthma disease prediction using naive Bayes—Neural network fusion technique," in *Parallel, Distributed and Grid Computing (PDGC), 2014 International Conference on*, 2014, pp. 137-140: IEEE.
- [2] I. Asher and N. Pearce, "Global burden of asthma among children," *The International Journal of Tuberculosis and Lung Disease*, vol. 18, no. 11, pp. 1269-1278, 2014.
- [3] G. A. Network, "The Global Asthma Report 2014," *Auckland, New Zealand*, 2014.
- [4] H. A. Ahmad, "Asma boleh dikawal," in *Harian Metro*, ed: Harian Metro, 2015, p. E30.
- [5] M. Al-khassaweneh, S. B. Mustafa, and F. Abu-Ekteish, "Asthma attack monitoring and diagnosis: A proposed system," in *Biomedical Engineering and Sciences (IECBES), 2012 IEEE EMBS Conference on*, 2012, pp. 763-767: IEEE.
- [6] H. Anderson, P. Bailey, J. Cooper, J. Palmer, and S. West, "Morbidity and school absence caused by asthma and wheezing illness," *Archives of Disease in Childhood*, vol. 58, no. 10, pp. 777-784, 1983.
- [7] A. M. Kwan *et al.*, "Personal Lung Function Monitoring Devices for Asthma Patients," *Sensors Journal, IEEE*, vol. 15, no. 4, pp. 2238-2247, 2015.
- [8] D. P. Abrahams, A. B. Ltd, Ed. *How the body works: A comprehensive illustrated encyclopedia of anatomy*. Wimbledo, London: Popular UK Pte Ltd, 2012, pp. 188-195.
- [9] E. G. Weinberg, "Urbanization and childhood asthma: an African perspective," *Journal of Allergy and Clinical Immunology*, vol. 105, no. 2, pp. 224-231, 2000.
- [10] N. Hijazi, B. Abalkhail, and A. Seaton, "Asthma and respiratory symptoms in urban and rural Saudi Arabia," *European Respiratory Journal*, vol. 12, no. 1, pp. 41-44, 1998.

- [11] F. L. Lim, Z. Hashim, L. T. L. Than, S. M. Said, J. H. Hashim, and D. Norbäck, "Asthma, airway symptoms and rhinitis in office workers in Malaysia: associations with house dust mite (HDM) allergy, cat allergy and levels of house dust mite allergens in office dust," *PloS one*, vol. 10, no. 4, p. e0124905, 2015.
- [12] B. Björkstén *et al.*, "Worldwide time trends for symptoms of rhinitis and conjunctivitis: Phase III of the International Study of Asthma and Allergies in Childhood," *Pediatric Allergy and Immunology*, vol. 19, no. 2, pp. 110-124, 2008.
- [13] P. Barry and C. o'Callaghan, "Multiple actuations of salbutamol MDI into a spacer device reduce the amount of drug recovered in the respirable range," *European Respiratory Journal*, vol. 7, no. 9, pp. 1707-1709, 1994.
- [14] O. Breuer, D. Shoseyov, E. Kerem, and R. Brooks, "Implementation of a Policy Change: Replacement of Nebulizers by Spacers for the Treatment of Asthma in Children," *The Israel Medical Association journal: IMAJ*, vol. 17, no. 7, p. 421, 2015.
- [15] G. Chaney, B. Clements, L. Landau, M. Bulsara, and P. Watt, "A new asthma spacer device to improve compliance in children: a pilot study," *Respirology*, vol. 9, no. 4, pp. 499-506, 2004.
- [16] A. Lahdensuo and A. Muittari, "Bronchodilator effects of a fenoterol metered dose inhaler and fenoterol powder in asthmatics with poor inhaler technique," *European journal of respiratory diseases*, vol. 68, no. 5, pp. 332-335, 1986.
- [17] AeroChamber, "AeroChamber Plus Flow-Vu Anti-Static Valved Holding Chamber," T. M. International, Ed., ed, 2016.
- [18] P. Pharmacy, "AeroChamber Plus* Flow-Vu* YELLOW," ed, 2015.
- [19] N. E. B. a. M. MPH, "The Global Asthma Report 2011," Paris, France2011.
- [20] U. Online, "Rakyat Malaysia tidak pandai kawal asma," in *Utusan Online* ed: Utusan Online 2016.
- [21] C. Kroegel, "Global Initiative for Asthma (GINA) guidelines: 15 years of application," *Expert review of clinical immunology*, vol. 5, no. 3, pp. 239-249, 2009.
- [22] McGraw-Hill, "Lower Respiratory Tract," ed, 2014.

- [23] R. L. Newell, "Anatomy of the post-laryngeal airways, lungs and diaphragm," *Surgery (Oxford)*, vol. 29, no. 5, pp. 199-203, 2011.
- [24] H. E. Houston, W. S. Payne, E. G. Harrison, and A. M. Olsen, "Primary cancers of the trachea," *Archives of Surgery*, vol. 99, no. 2, pp. 132-140, 1969.
- [25] N. T. A. System, "Upper Respiratory: Cross section of the trachea," ed, 2015.
- [26] M. Ochs *et al.*, "The number of alveoli in the human lung," *American journal of respiratory and critical care medicine*, vol. 169, no. 1, pp. 120-124, 2004.
- [27] A. Hislop, J. Wigglesworth, and R. Desai, "Alveolar development in the human fetus and infant," *Early human development*, vol. 13, no. 1, pp. 1-11, 1986.
- [28] Colleen, "Each bronchiole terminates in an alveolar sac, a group of alveoli," ed, 2012.
- [29] C. G. Lausted, A. T. Johnson, W. H. Scott, M. M. Johnson, K. M. Coyne, and D. C. Coursey, "Maximum static inspiratory and expiratory pressures with different lung volumes," *Biomedical engineering online*, vol. 5, no. 1, p. 1, 2006.
- [30] S. Gupta and S. M. Donn, "Continuous positive airway pressure: Physiology and comparison of devices," in *Seminars in Fetal and Neonatal Medicine*, 2016, vol. 21, no. 3, pp. 204-211: Elsevier.
- [31] L. E. Kerper, H. N. Lynch, K. Zu, G. Tao, M. J. Utell, and J. E. Goodman, "Systematic review of pleural plaques and lung function," *Inhalation toxicology*, vol. 27, no. 1, pp. 15-44, 2015.
- [32] H. A. Jenkins, R. Cherniack, S. J. Szeffler, R. Covar, E. W. Gelfand, and J. D. Spahn, "A comparison of the clinical characteristics of children and adults with severe asthma," *CHEST Journal*, vol. 124, no. 4, pp. 1318-1324, 2003.
- [33] Donald.C.Rizzo, *Fundamentals of Anatomy and Physiology*. Delmar, Cengage Learning, 2010.
- [34] Megan, "BIO 202 Respiratory System Worksheet," ed, 2012.
- [35] S. Arqam M. , "How does the structure of the alveoli relate to its function in the lungs?," ed, 2015.
- [36] P. G. Gibson, M. Abramson, R. Wood-Baker, J. Volmink, M. Hensley, and U. Costabel, *Evidence-based respiratory medicine*. John Wiley & Sons, 2008.

- [37] C. Ober and T. C. Yao, "The genetics of asthma and allergic disease: a 21st century perspective," *Immunological reviews*, vol. 242, no. 1, pp. 10-30, 2011.
- [38] N. Papadopoulos *et al.*, "International consensus on (ICON) pediatric asthma," *Allergy*, vol. 67, no. 8, pp. 976-997, 2012.
- [39] R. S. Peebles, "Viral infections, atopy, and asthma: is there a causal relationship?," *Journal of allergy and clinical immunology*, vol. 113, no. 1, pp. S15-S18, 2004.
- [40] E. K. Miller *et al.*, "Host and viral factors associated with severity of human rhinovirus-associated infant respiratory tract illness," *Journal of Allergy and Clinical Immunology*, vol. 127, no. 4, pp. 883-891, 2011.
- [41] R. F. Lemanske, "The childhood origins of asthma (COAST) study," *Pediatric Allergy and Immunology*, vol. 13, no. s15, pp. 38-43, 2002.
- [42] C. Murray, S. Pipis, E. McArdle, L. Lowe, A. Custovic, and A. Woodcock, "National Asthma Campaign-Manchester Asthma and Allergy Study Group. Lung function at one month of age as a risk factor for infant respiratory symptoms in a high risk population," *Thorax*, vol. 57, no. 5, pp. 388-392, 2002.
- [43] E. f. Health, "Asthma Pathology of asthma," ed, 2015.
- [44] P. B. Myrdal, P. Sheth, and S. W. Stein, "Advances in metered dose inhaler technology: formulation development," *AAPS PharmSciTech*, vol. 15, no. 2, pp. 434-455, 2014.
- [45] S. P. Newman, *Respiratory drug delivery: essential theory and practice*. Respiratory Drug Delivery Online, 2009.
- [46] S. Long *et al.*, "Multi-wall carbon nanotubes film used for determination of salbutamol sulfate," 2009.
- [47] F. M. Ducharme, M. Ni Chroinin, I. Greenstone, and T. J. Lasserson, "Addition of long-acting beta2-agonists to inhaled corticosteroids versus same dose inhaled corticosteroids for chronic asthma in adults and children," *Cochrane Database Syst Rev*, vol. 5, no. 5, p. CD005535, 2010.
- [48] A. J. Wood and H. S. Nelson, " β -Adrenergic bronchodilators," *New England Journal of Medicine*, vol. 333, no. 8, pp. 499-507, 1995.
- [49] A. Jantikar *et al.*, "Comparison of bronchodilator responses of levosalbutamol and salbutamol given via a pressurized metered dose inhaler: a randomized, double

- blind, single-dose, crossover study," *Respiratory medicine*, vol. 101, no. 4, pp. 845-849, 2007.
- [50] G. P. Polli, W. M. Grim, F. A. Bacher, and M. H. Yunker, "Influence of formulation on aerosol particle size," *Journal of pharmaceutical sciences*, vol. 58, no. 4, pp. 484-486, 1969.
- [51] S. P. Newman, "Principles of metered-dose inhaler design," *Respiratory care*, vol. 50, no. 9, pp. 1177-1190, 2005.
- [52] A. S. o. Canada, "How to Use Your Inhaler?," ed, 2016.
- [53] D. Lewis, D. Ganderton, B. Meakin, and G. Brambilla, "Theory and practice with solution systems," *Respir Drug Deliv*, vol. 1, pp. 109-16, 2004.
- [54] C. Thiel, "From Susie's question to CFC free: an inventor's perspective on forty years of MDI development and regulation," *Respiratory Drug Delivery V. Interpharm Press, Buffalo Grove, IL*, vol. 115123, 1996.
- [55] T. Noakes, "Medical aerosol propellants," *Journal of fluorine chemistry*, vol. 118, no. 1, pp. 35-45, 2002.
- [56] M. J. Molina and F. S. Rowland, "Stratospheric sink for chlorofluoromethanes: chlorine atom-catalysed destruction of ozone," *Nature*, vol. 249, no. 28, pp. 810-812, 1974.
- [57] K. J. McDonald and G. P. Martin, "Transition to CFC-free metered dose inhalers—into the new millennium," *International journal of pharmaceuticals*, vol. 201, no. 1, pp. 89-107, 2000.
- [58] B. J. Lipworth, D. K. Lee, J. Anhøj, and H. Bisgaard, "Effect of plastic spacer handling on salbutamol lung deposition in asthmatic children," *British journal of clinical pharmacology*, vol. 54, no. 5, pp. 544-547, 2002.
- [59] C. J. Hallberg, M. T. Lysaught, C. E. Zmudka, W. K. Kopesky, and L. E. Olson, "Characterization of a human powered nebulizer compressor for resource poor settings," *Biomedical engineering online*, vol. 13, no. 1, p. 77, 2014.
- [60] M. Cheţan and A. Negoiaş, "New approaches to nebulizer drug delivery," in *Advanced Topics in Electrical Engineering (ATEE), 2011 7th International Symposium on*, 2011, pp. 1-4: IEEE.

- [61] A. Amani, P. York, H. Chrystyn, and B. J. Clark, "Evaluation of a nanoemulsion-based formulation for respiratory delivery of budesonide by nebulizers," *AAPS PharmSciTech*, vol. 11, no. 3, pp. 1147-1151, 2010.
- [62] A. Yardimci, "Microcontroller based jet nebulizer design with ANFIS compressor control for domiciliary use," in *Innovations in Intelligent Systems and Applications (INISTA), 2011 International Symposium on*, 2011, pp. 428-431: IEEE.
- [63] C.-C. Chen *et al.*, "Low-cost electronic dose counter for pressurized metered dose inhaler," in *Consumer Electronics-Taiwan (ICCE-TW), 2015 IEEE International Conference on*, 2015, pp. 400-401: IEEE.
- [64] G. Assam, "Metered Dose Inhaler: A Review," *International Research Journal of Pharmaceutical and Applied Sciences (IRJPAS)*, vol. 3(1), pp. 37-45, 2013.
- [65] J. Pilcher *et al.*, "Validation of a metered dose inhaler electronic monitoring device: implications for asthma clinical trial use," *BMJ Open Respiratory Research*, vol. 3, no. 1, p. e000128, 2016.
- [66] M. Patel, J. Pilcher, A. Chan, K. Perrin, P. Black, and R. Beasley, "Six-month in vitro validation of a metered-dose inhaler electronic monitoring device: implications for asthma clinical trial use," *Journal of Allergy and Clinical Immunology*, vol. 130, no. 6, pp. 1420-1422, 2012.
- [67] N. J. Bowman, M. J. Holroyd, C. Panayi, and W. R. Treneman, "Inhaler dose counter," ed: Google Patents, 2002.
- [68] P. Buddiga, "Use of Metered Dose Inhalers, Spacers, and Nebulizers," ed, 2015.
- [69] G. K. Crompton, "How to achieve good compliance with inhaled asthma therapy," *Respiratory medicine*, vol. 98, pp. S35-S40, 2004.
- [70] T. E. Taylor, M. S. Holmes, I. Sulaiman, S. D'Arcy, R. W. Costello, and R. B. Reilly, "An acoustic method to automatically detect pressurized metered dose inhaler actuations," in *Engineering in Medicine and Biology Society (EMBC), 2014 36th Annual International Conference of the IEEE*, 2014, pp. 4611-4614: IEEE.
- [71] D. Von Hollen, E. Lieberman, J. Paine, and M. Paine, "Actuator for a metered dose inhaler," ed: Google Patents, 2006.

- [72] K. Otsuka and C. M. Wayman, *Shape memory materials*. Cambridge university press, 1999.
- [73] N. S. B. Azlan, "Humidity and Gas Sensor Monitoring System for Tenaga Nasional Berhad Substation Battery Room by Using Microcontroller " Bachelor Degree in Electronic Engineering with Honours, Faculty of Electronic and Electrical Engineering Universiti Tun Hussein Onn Malaysia (UTHM), 2013.
- [74] A. A. B. M. Rozimi, "Pembangunan Sistem Pengesan Gas Mudah Alih Dengan Menggunakan Sensor Gas Untuk Dalam Rumah," Bachelor Degree in Electronic Engineering with Honours, Faculty of Electronic and Electrical Engineering, Universiti Tun Hussein Onn Malaysia (UTHM), 2014.
- [75] W. Ding, R. Hayashi, J. Suehiro, K. Imasaka, and M. Hara, "Observation of dynamic behavior of PD-generated SF 6 decompositions using carbon nanotube gas sensor," in *Electrical Insulation and Dielectric Phenomena, 2005. CEIDP'05. 2005 Annual Report Conference on*, 2005, pp. 561-564: IEEE.
- [76] A. Shrivastava, R. Prabhaker, R. Kumar, and R. Verma, "GSM Based Gas Leakage Detecton System," *International Journal of Emerging Trends in Electrical and Electronics (IJETEE-ISSN: 2320-9569)*, vol. 3, no. 2, 2013.
- [77] S. Shinde, S. Patil, and A. Patil, "Development of movable gas tanker leakage detection using wireless sensor network based on embedded system," *International Journal of Engineering Research and Application (IJTERA)*, vol. 2, pp. 1180-1183, 2012.
- [78] K. P. Priya, M. Surekha, R. Preethi, T. Devika, and N. Dhivya, "Smart Gas Cylinder Using Embedded System," *International Journal of Innovative Research in Electrical, Electronics, Instrumentation and Control Engineering (IJIREEICE) Vol*, vol. 2, pp. 958-962, 2014.
- [79] X. Liu, S. Cheng, H. Liu, S. Hu, D. Zhang, and H. Ning, "A survey on gas sensing technology," *Sensors*, vol. 12, no. 7, pp. 9635-9665, 2012.
- [80] S. M. Kanan, O. M. El-Kadri, I. A. Abu-Yousef, and M. C. Kanan, "Semiconducting metal oxide based sensors for selective gas pollutant detection," *Sensors*, vol. 9, no. 10, pp. 8158-8196, 2009.

- [81] M. Batzill and U. Diebold, "The surface and materials science of tin oxide," *Progress in surface science*, vol. 79, no. 2, pp. 47-154, 2005.
- [82] H.-E. Endres *et al.*, "A thin-film SnO₂ sensor system for simultaneous detection of CO and NO₂ with neural signal evaluation," *Sensors and Actuators B: Chemical*, vol. 36, no. 1-3, pp. 353-357, 1996.
- [83] U. Hoefer, H. Böttner, A. Felske, G. Kühner, K. Steiner, and G. Sulz, "Thin-film SnO₂ sensor arrays controlled by variation of contact potential—a suitable tool for chemometric gas mixture analysis in the TLV range," *Sensors and Actuators B: Chemical*, vol. 44, no. 1, pp. 429-433, 1997.
- [84] F. Berger, J.-B. Sanchez, and O. Heintz, "Detection of hydrogen fluoride using SnO₂-based gas sensors: Understanding of the reactional mechanism," *Sensors and Actuators B: Chemical*, vol. 143, no. 1, pp. 152-157, 2009.
- [85] H. E. C. LTD. (1st April). *MQ-4 Gas Sensor*. Available: <https://www.sparkfun.com/datasheets/Sensors/Biometric/MQ-4.pdf>
- [86] H. E. C. LTD. *MQ-5 Gas Sensor*. Available: <https://www.parallax.com/sites/default/files/downloads/605-00009-MQ-5-Datasheet.pdf>
- [87] H. Sensors, "MQ-6 Gas Sensor," *MQ-6 datasheet*.
- [88] T. A. Emadi, C. Shafai, M. S. Freund, D. J. Thomson, D. S. Jayas, and N. D. White, "Development of a polymer-based gas sensor-humidity and CO₂ sensitivity," in *Microsystems and Nanoelectronics Research Conference, 2009. MNRC 2009. 2nd*, 2009, pp. 112-115: IEEE.
- [89] H. Bai and G. Shi, "Gas sensors based on conducting polymers," *Sensors*, vol. 7, no. 3, pp. 267-307, 2007.
- [90] K. K. Wong, Z. Tang, J. K. Sin, P. C. H. Chan, P. W. Cheung, and H. Hiraoka, "Study on selectivity enhancement of tin dioxide gas sensor using non-conducting polymer membrane," in *Electron Devices Meeting, 1995., Proceedings 1995 IEEE Hong Kong*, 1995, pp. 42-45: IEEE.
- [91] B. C. Munoz, G. Steinthal, and S. Sunshine, "Conductive polymer-carbon black composites-based sensor arrays for use in an electronic nose," *Sensor Review*, vol. 19, no. 4, pp. 300-305, 1999.

- [92] T. T. Thai, L. Yang, G. R. DeJean, and M. M. Tentzeris, "Nanotechnology enables wireless gas sensing," *IEEE Microwave Magazine*, vol. 12, no. 4, pp. 84-95, 2011.
- [93] A. Mehdipour, I. D. Rosca, A. Sebak, C. Trueman, and S. Hoa, "Advanced carbon-fiber composite materials for RFID tag antenna applications," *Appl. Comput. Electromagn. Soc.(ACES) J*, vol. 25, no. 3, 2010.
- [94] L. Yang, R. Zhang, D. Staiculescu, C. Wong, and M. M. Tentzeris, "A novel conformal RFID-enabled module utilizing inkjet-printed antennas and carbon nanotubes for gas-detection applications," *IEEE Antennas and Wireless Propagation Letters*, vol. 8, pp. 653-656, 2009.
- [95] K. G. Ong, K. Zeng, and C. A. Grimes, "A wireless, passive carbon nanotube-based gas sensor," *IEEE Sensors Journal*, vol. 2, no. 2, pp. 82-88, 2002.
- [96] Y. Miao, Q. Yao, N. Qiu, and J. Zhang, "Application research of laser gas detection technology in the analysis of Sulphur hexafluoride," in *Electricity Distribution (CICED), 2010 China International Conference on*, 2010, pp. 1-3: IEEE.
- [97] T. C. Bond, G. D. Cole, L. L. Goddard, and E. M. Behymer, "Photonic MEMS for NIR in-situ Gas Detection and Identification," in *Sensors, 2007 IEEE*, 2007, pp. 1368-1371: IEEE.
- [98] Z. Haiming, "Experiment study of continuous emission monitoring system based on differential optical absorption spectroscopy," in *Education Technology and Training, 2008. and 2008 International Workshop on Geoscience and Remote Sensing. ETT and GRS 2008. International Workshop on*, 2008, vol. 1, pp. 175-177: IEEE.
- [99] Y. Wang, K. Wang, Q. Wang, and F. Tang, "Measurement of CH₄ by differential infrared optical absorption spectroscopy," in *Proceedings of the 9th International Conference on Electronic Measurement & Instruments*, 1766, vol. 2009.
- [100] H. Miya *et al.*, "Compact Raman Lidar for hydrogen gas leak detection," in *Conference on Lasers and Electro-Optics/Pacific Rim*, 2009, p. ME1_3: Optical Society of America.
- [101] E. McNaghten, A. Parkes, B. Griffiths, A. Whitehouse, and S. Palanco, "Detection of trace concentrations of helium and argon in gas mixtures by laser-induced

- breakdown spectroscopy," *Spectrochimica Acta Part B: Atomic Spectroscopy*, vol. 64, no. 10, pp. 1111-1118, 2009.
- [102] G. Hallewell, G. Crawford, D. McShurley, G. Oxoby, and R. Reif, "A sonar-based technique for the ratiometric determination of binary gas mixtures," *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment*, vol. 264, no. 2-3, pp. 219-234, 1988.
- [103] S. Minglei, L. Xiang, Z. Changping, and Z. Jiahua, "Gas concentration detection using ultrasonic based on wireless sensor networks," in *Information Science and Engineering (ICISE), 2010 2nd International Conference on*, 2010, pp. 2101-2106: IEEE.
- [104] S. Jacobson, "New developments in ultrasonic gas analysis and flowmetering," in *Ultrasonics Symposium, 2008. IUS 2008. IEEE*, 2008, pp. 508-516: IEEE.
- [105] M. Sonoyama, Y. Kato, and H. Fujita, "Application of ultrasonic to a hydrogen sensor," in *Sensors, 2010 IEEE*, 2010, pp. 2141-2144: IEEE.
- [106] K.-H. Kim, "Performance characterization of the GC/PFPD for H₂S, CH₃SH, DMS, and DMDS in air," *Atmospheric Environment*, vol. 39, no. 12, pp. 2235-2242, 2005.
- [107] C. Caucheteur, M. Debliquy, D. Lahem, and P. M  gret, "Catalytic fiber Bragg grating sensor for hydrogen leak detection in air," *IEEE Photonics Technology Letters*, vol. 20, no. 2, pp. 96-98, 2008.
- [108] P. Tardy, J.-R. Coulon, C. Lucat, and F. Menil, "Dynamic thermal conductivity sensor for gas detection," *Sensors and Actuators B: Chemical*, vol. 98, no. 1, pp. 63-68, 2004.
- [109] Y. A. Badamasi, "The working principle of an Arduino," in *Electronics, Computer and Computation (ICECCO), 2014 11th International Conference on*, 2014, pp. 1-4: IEEE.